REMARKS/ARGUMENTS

Claims 14, 15, 18 through 20, 22, 23, 32 through 34, 36 through 43 and 45 through 51are pending in the application

Applicant respectfully requests that the following remarks be considered in view of the Office Action made Final.

Rejection of Claims 14, 15, 18 through 20, 22, 23, 32 through 34, 36 through 43 and 45 through 51 Under 35 USC § 103(a)

Claims 14, 15, 18 through 20, 22, 23, 32 through 34, 36 through 43 and 45 through 51 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent Publication No. 2005/0025756 Erwin (hereinafter "Erwin") further in view of Soft Gel Technologies, Inc. EP 888774 (hereinafter "Soft Gel") and U.S. Patent Publication No. 2004/0001874 Davidson et al. (hereinafter "Davidson"). Applicant respectfully traverses the rejection for at least the following reasons.

Erwin Is Not Prior Art To The Instant Invention

Attached hereto, as Appendix I, is a 37 C.F.R. § 1.131 declaration from the inventor of the instant invention, Mr. Michael Fantuzzi. Attached along with the declaration are pages from Mr. Fantuzzi's lab notebooks and emails with his colleagues dated from the period between March 14, 2003 to August 22, 2003. As declared by Mr. Fantuzzi and as evidenced by the materials in the appendix, Mr. Fantuzzi conceived of the invention at least as early as March 13, 2003. Mr. Fantuzzi's conception was followed by diligent reduction to practice followed by filing of U.S. utility application Serial No.: 10/674,268 on September 29, 2003. The earliest priority date Erwin can claim is June 25, 2003 based on the filing of U.S. provisional application 60/482,781 which is devoid of any data and provides only prophetic examples. Thus, the instant invention, showing prior conception and reduction to practice, pre-dates Erwin. Erwin is therefore not prior art to the instant invention.

Erwin Is Not Enabled And Provides Conflicting Statements

On page 3 of the Office Action, the Office cites to Erwin for the proposition that Erwin discloses that CoQ-10 is soluble in limonene, as well as in a number of lipophilic solvents, which are various plant oils, fatty acids and fatty acid esters including the vitamin E ester, tocopheroyl acetate. However, Erwin is ineffective to establish any disclosure regarding the solubility of CoQ-10 in any solvent or dispersion for at least the following reasons.

Erwin is not enabled for the effect of any solvent on CoQ-10. Erwin is entirely prophetic in its single example and is completely lacking of data. While, in some cases, such prophetic examples may provide insight to those of skill in the art, in the instant case, Erwin makes statements that are contradicted by real data provided in the prior art. Thus, lacking any support for statements made, Erwin would not supply any assistance in providing a solvent that is physiologically safe and also effective with CoQ-10.

Specifically, the Office states that Erwin discloses the CoQ-10 is soluble in a number of lipophilic solvents including plant oils, fatty acids and fatty acid esters. However, the present invention discloses (and provides data) showing that surprisingly, at least up to about 60% w/w CoQ-10 is soluble in d-limonene without heating. The Office, accepting the undocumented statements of Erwin, states that Erwin discloses that CoQ-10 is soluble in a number of lipohilic solvents including plant oils, fatty acids and fatty acid esters. However, the Office's attention is directed to Kommuru et al. (Int. J Pharm. 2001 Jan 16;212(2):233-46.) which includes actual data showing the results of controlled experiments investigating the solubility of CoQ-10 in various vegetable oils. In all cases, the solubility of CoQ-10 in naturally occurring vegetable oils is only about 8% w/v (approximately 9% w/w) several fold less than that for which data is provided in the instant invention. Further, Kommuru et al. also investigate the solubility in synthetic oils such as Myvacet 9-45, Captex-200 and Neobee M-5 (including fatty acids and esters alluded to by the Office). These compounds only increase the solubility of CoQ-10 up to 16.9% w/w. Further, the protocols for solubility including heating the mixtures at 60 °C with vortexing. Thus, those of skill in the art reading the disclosure of Erwin (which lacks any data) would know that the solubility of CoQ-10 in vegetable oils does not exceed about 8 % w/w, as is reported by Folkers, Kommuru and the instant application. See, para. [0007].

Further, contrary to the Office's assertion that fish oil is a fatty–acid containing lipophilic solvent, it is clear that lipophilicity plays only a small part in the solubility of CoQ-10. For example, the Offices attention is directed to Folkers et al., U.S. Patent No. 4,824,669. Folkers discloses a 1 ml fat emulsion of CoQ-10 (30 μg, 15 μg and 7.5 μg) e.g. an emulsion of CoQ-10 of *only 3%* w/v when initially suspended in soy oil falling to 0.003%, 0.0015% and 0.0007.5 % when made into the emulsions disclosed in col. 6, lines 43-46. Further, applicants point out that Folkers teaches that the CoQ-10 remains in the oil phase of the composition and does not partition into the lipid carrier. (Folkers, Col. 6, lines 63-66). This partition occurs even after the emulsion was sonicated and subjected to shearing by passing the emulsion between two syringes connected by tubing. These actual results, therefore, directly refute the Office's contention that "Erwin discloses that co Q10 is soluble in limonene as well as in a number of lipophilic (or hydrophobic) solvents." Further highlighting the limitation of lipid as solvents, Folkers teaches that "CoQ_{10} levels above about 30 μg/ml (e.g. 0.003%)" are unstable. Col. 5, lines 34-35. Thus, directly teaching away from the ability to provide more absorbable CoQ-10 per dose than the 30 μg described by Folkers in a lipid carrier.

Further, Folkers, in discussing gelatin capsules of CoQ-10 manufactured by Scherer North American, identifies that the gel capsules contain 33.3 mg of pure CoQ-10 in 400 mg of Soybean oil, e.g., a composition of, at most, 8.32% w/v (all vegetable oils have a density of approximately 0.92 (See Appendix II, Density of Cooking Oils). E.g., the soft gel capsule disclosed by Folkers has a composition of CoQ-10 of only approximately 9.0 % w/w. Thus, the concentration of approximately 60% w/w disclosed in the instant invention comprises a solubility in d-limonene much greater than anything possible in soy oil or other reporter oil or surfactant.

Therefore, one of skill in the art at the time the invention was made would not know in reading the undocumented and prophetic disclosure of Erwin, that limonene would provide any greater solubility for CoQ-10 than previous reports by Folkers and Soft Gel. Thus, the Office's statement on page 3 of the Office Action that "Erwin provide the expectation that one could dissolve CoQ-10 in a solvent that is a lipid or that is hydrophobic" is inapposite, to be generous.

Soft Gel Does Not Teach A Solvent Capable Of Producing A Solution Of Greater Than 8% W/W

With regard to Soft Gel, the Office states that "if the co Q10 were not soluble in the rice bran oil, a precipitate would form. In that event, the liquid- the rice bran oil- could not have been manipulated to produce uniform soft gel capsules for dose control." However, again the Office's attention is directed to Folkers because Folkers teaches an injectable suspension of CoQ-10. Folkers specifically states that, in order to get the CoQ-10 into a soy emulsion, the components are sonicated and then passed back and forth between the needles of syringes to provide "microspheres" of oil in the emulsion in which the CoQ10 was "presumed" to be dissolved. See, col. 6, lines 63-66. This, in spite of the fact that the emulsions contained only concentrations of CoQ10 ranging from 0.003%, 0.0015% and 0.0007.5 % w/v (two to three orders of magnitude less than the present invention). This data directly refutes the Office's statement that "[A]lthough the two solvents, limonene and rice bran oil, have different chemical structures, both can be used to prepare solution of co Q10. Thus, they are functional equivalents and may be used interchangeably." Applicant notes that a liquid that can be used to provide a solution of up to 60% w/w without heating is not the functional equivalent of a liquid that can only provide a solubility of 8 % with heating. Such liquids could not be used interchangeably.

In addition, the Office reads into Soft Gel the element that CoQ-10 is miscible or dissolved therein "[O]therwise, . . . the soft gel could not have been manipulated to produce uniform soft gel capsules." However, Folkers teaches an intravenous preparation of CoQ-10 which clearly partitions into an oil phase even after robust mechanical manipulation. Thus, if Folkers could produce a uniform preparation of suspended CoQ-10 in a two-phase solution for *intravenous* administration, the ability to produce a suspended preparation of CoQ-10 in fish oil for encapsulation in soft gels is not surprising and does not require the inclusion of limitations that are not in the specification. Therefore, for at least these reasons, the rejection is overcome and should be withdrawn.

Davidson Does Not Provide The Missing Elements

The Office asserts that Davidson implies that CoQ-10 is soluble in fish oil even though the reference uses the term "blend". Applicant, points out that Davidson chose to use the word "blend". Davidson did not choose to use the words "dissolve" or "solubilize". Applicant points

out that the definition of blend is: "to mix or combine together." Applicants point out that the definition of solubilize is: "to pass into a solution". The two words are not interchangeable in the world of chemistry. The Office is not simply free to exchange the meaning of one word for another. Further, Applicants point out that Folkers explicitly states that he is unsure whether CoQ-10 was dissolved in the emulsion (at a concentration of 0.003%, 0.0015% and 0.0007.5 % w/v). Therefore, it is unclear how Davidson teaches anything about the solubility of CoQ-10 solublized in fish oil much less limonene. Therefore, for at least this reason, the rejection over Davidson is overcome and should be withdrawn.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the above, Applicant respectfully submits that the present application is in condition for allowance. Reconsideration of the present application and a favorable response are respectfully requested.

If a telephone conference would be helpful in resolving any remaining issues, please contact the following at (612) 492-6864.

No fee is deemed necessary. However, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment and notify us of same, to Deposit Account No. 04-1420.

Respectfully submitted,

DORSEY & WHITNEY LLP

Customer Number 25763

Date: October 8, 2007

By: _____

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